UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P O Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
|---|---|---|---|---|
| 10/564,273 | 07/31/2007 | Jakov Vaisman | 64734(70403) | 6986 |

21874 7590 10/06/2009

EDWARDS ANGELL PALMER & DODGE LLP
P.O. BOX 55874
BOSTON, MA 02205

| EXAMINER | |
|---|---|
| BETTON, TIMOTHY E | |

| ART UNIT | PAPER NUMBER |
|---|---|
| 1617 | |

| MAIL DATE | DELIVERY MODE |
|---|---|
| 10/06/2009 | PAPER |

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 10/564,273 | VAISMAN, JAKOV | |
| | Examiner | Art Unit | |
| | TIMOTHY E. BETTON | 1617 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *11 May 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *62,63,66,69-80 and 82-84* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *62,63,66,69-80 and 82-84* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

**DETAILED ACTION**

Applicant' Remarks filed on 11 May 2009 has been acknowledged and duly made of record.

Rejections not reiterated from previous Office Actions are hereby withdrawn. The following rejections are either reiterated or newly applied. They constitute the complete set presently being applied to the instant application.

The opinion evidence as discussed on page 9 of applicants' response filed on 11 May 2009 notes :

As disclosed in the present specification, the Applicant has surprisingly found that by **splitting the routes of administration**, an increased level of satisfaction is experienced by patients suffering from premature ejaculation. The symbol ++ in the table at page 15 of the specification relates to a measure of satisfaction, **which is not a quantitative measure**. It is believed (without wishing to be bound by theory), based upon clinical observation, that by splitting the routes of administration, the medicament can absorb rapidly into the central nervous system and, at the same time, act on the nerve endings in the penis to provide partial desensitization. This effect is otherwise not achievable if the antidepressant is administered via only one route. This is neither taught nor disclosed in the cited prior art. This effect is also unexpected and unpredictable.

The specification at page 14 only provides the following support for the experimental procedure:

Antidepressants were administered to a large number of subjects in accordance with the method of the present invention. The study involved in excess of 200 patients in each treatment group. All subjects reported experiencing premature ejaculation prior to commencing the study**. All medicaments were self administered.** Topical administration was to the skin of the glans. Paroxetine, Fluoxetine and Sertraline were administered randomly via a mixture of routes.

Applicant's arguments have been considered but are not deemed persuasive. The data is not quantitative, and the experimental parameters for determining what ++ means versus + are unclear. It is unclear how satisfaction is determined or measured, and what it means by quantifiable data. The Table at page 15 provides no data of both statistical and practical

significance upon which to base a conclusion of superiority of the claimed methods. There is no indication of what is the line of distinction between a score of + versus one of ++. If the subjects were given a questionnaire to assess satisfaction, the nature of that questionnaire in determining this distinction (if any) is not given. This information provided in the specification is nothing more than an opinion with poorly described experimental procedures and vague conclusions. For instance, there is no assessment of what positive psychological effect the simple act of self-administering the compositions by the ++ group contributes to the outcome. A proper control would be to administer the medicament nasally and provide a placebo for the topical administration, then compare those results to the ++ group who received medicament in both applications nasally and topically. Another control experiment would be to provide placebo in the nasal medicament and active ingredients in the medicament used topically. Then a proper assessment via the same questionnaire, for example, might demonstrate a significant distinction in the determination of levels of satisfaction between the two groups and show that there is a benefit unexpectedly achieved through the administration of two medicaments via the nasal and topical routes.

Regarding opinion evidence, see MPEP 716.01 (c), Part III. Note particularly *In re Beattie*, 974 F.2d 1309, 24 USPQ2d 1040 (Fed. Cir. 1992) (declarations of seven persons skilled in the art offering opinion evidence praising the merits of the claimed invention were found to have little value because of a lack of factual support) and *Ex parte George*, 21 USPQ2d 1058 (Bd. Pat. App. & Inter. 1991) (conclusory statements that results were "unexpected," unsupported by objective factual evidence, were considered but were not found to be of

substantial evidentiary value). See also MPEP 716.02(a), Parts I-III regarding the burden of applicant to establish unexpected results for their invention:

The evidence relied *>upon< should establish "that the differences in results are in fact unexpected and unobvious and of both statistical and practical significance." Ex parte Gelles, 22 USPQ2d 1318, 1319 (Bd. Pat. App. & Inter. 1992) (Mere conclusions in appellants' brief that the claimed polymer had an unexpectedly increased impact strength "are not entitled to the weight of conclusions accompanying the evidence, either in the specification or in a declaration."); Ex parte C, 27 USPQ2d 1492 (Bd. Pat. App. & Inter. 1992) (Applicant alleged unexpected results with regard to the claimed soybean plant, however there was no basis for judging the practical significance of data with regard to maturity date, flowering date, flower color, or height of the plant.). See also In re Nolan, 553 F.2d 1261, 1267, 193 USPQ 641, 645 (CCPA 1977) and In re Eli Lilly, 902 F.2d 943, 14 USPQ2d 1741 (Fed. Cir. 1990) as discussed in MPEP §716.02(c).

***Claim Rejections - 35 USC § 112***

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 76-80 and 82-84 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The limitation drawn to a medicament for the treatment of premature ejaculation is unclear because it is uncertain as to if medicaments are referring to separate formulations, respectively or medicaments in a concomitant formulation.

On page 14 of the specification, the following is disclosed:

Antidepressants were administered to a large number of subjects in accordance with the method of the present invention. The study involved in excess of 200 patients in each treatment group. All subjects reported experiencing premature ejaculation prior

to commencing the study**. All medicaments were self administered.** Topical administration was to the skin of the glans. Paroxetine, Fluoxetine and Sertraline were administered randomly via a mixture of routes.

However, in the instant claim set, claim 76 specifically discloses:

76. (Currently amended) A medicament for the treatment of premature ejaculation, **said medicament composition consisting of an antidepressant formulated for nasal administration and an antidepressant formulated for local administration to at least part of the male genitalia.**

Thus, the portion in the specification *supra* fails to disclose the distinction drawn to medicaments as found in instant claim 76. Based upon the context in which the term *medicament* is disclosed within the specification absent of any definition to clearly delineate, it would not be readily apparent to the one of skill to administer one agent as a medicament as opposed to two or more agents as a medicament unit. The term *medicament composition* as found in claim 76 suggests that this is a single composition consisting of two antidepressants formulated for two different intended uses: one for nasal administration and the other for administration to the genitalia. While one composition may be capable of performing both tasks, the specification at page 14 seems to indicate this claim language is not what is intended. Because claim 76 and dependent claims are vague and indefinite, these claims will be interpreted to mean a single composition formulated capable of both intended uses. If applicant intends these formulations to be separate, then this distinction should be made.

### *Claim Rejections - 35 USC § 112*

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 73 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Specifically, it is unclear as to whether the massaging is occurring for one minute or is the intercourse lasting for one minute.

Applicant should move the phrase "for about one minute" after the word "genitalia". Please see claim 74 for an example of the correct grammatical construction.

***Claim Rejections - 35 USC § 102***

> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 76, 77, 79 are rejected under 35 U.S.C. 102(b) as being anticipated by Altabet (USPN 6, 943, 193 B1).

Altabet teaches atomoxetine, an antidepressant for treating premature ejaculation. See column 5, lines 29-32. Various formulations for administration by **nasal**, transdermal (i.e. skin patch), and percutaneous, intravenous, intramuscular or intrarectal delivery methods are taught. Formulations for these delivery methods may be prepared by any of the methods well known in the art of pharmacy (col. 6, lines 39-43). In particular, see column 6, lines 4-10, where pharmaceutical formulations using any pharmaceutically acceptable carrier can be made. This

includes liquids and various oral or nasal forms. See column 5, lines 51-60. Water is inherently part of pharmaceutically acceptable carrier known in the art, and is capable of providing a formulation that can be used both for nasal administration and administration to the genitalia.

Thus, Altabet anticipates the limitations of claims 76, 77, 79 and 82.

***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any

evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 62-63, 66, and 69-75 are rejected under 35 U.S.C. 103(a) as being unpatentable over Bar-Or (USPGPUB 2002/0132857 A1) in view of Crenshaw et al. (USPN 5151448), and Rojas-Corrales et al. [Journal of Psychopharmacology 18(3):404-411 (2004)].

Bar-Or teaches that formulations were known in the prior art using anti-depressants, and that choosing which one to use would be driven by effective response in a given patient. The combination of any known effective antidepressants would have been obvious in view of Kerkhoven (especially since it may require determining specific combinations that are effective in a given patient. This would have been obvious to the skilled artisan. Further, it is asserted that the claims that are drawn to the administration directly to the genitalia for specific time periods to be obvious in view of the teachings of transdermal delivery of the medicaments taught in the prior art. These limitations (application to the genitalia for specific time periods) are not deemed to provide a distinction over the teachings of the prior art for transdermal delivery. Simultaneous deliver via two different methods would have been obvious, as it was known in the art that delivery through the skin versus the mucous membrane of the nose would deliver different effective amounts of the medicament. Nasal delivery will provide for a faster delivery to the bloodstream, while a transdermal delivery can provide a slower, sustained release of the medicament through the skin as an advantage for patients also requiring a steady dose of

medicament over a longer period of time following the initial burst of drug. In this regard, applicant points to the opinion evidence in the specification at pages 14 and 15.

Bar-Or reference teaches Tramadol. Bar-Or paragraphs 4-7 in the context of treatment of premature ejaculation using anti-depressants, teaches that although Bar-Or seems to suggest problems with the use of antidepressants for treating premature ejaculation, this caution is only that the particular antidepressants of the prior art may not be effective for all patients. See paragraph 5, lines 6-7. Tramadol is suggested as a new treatment option. In fact, Tramadol is inherently also an antidepressant.

Bar-Or also teach that this composition may be optimized to be given topically (see paragraph 20 at line 4).

The following is cited only as EVIDENCE of inherency of the prior art product. See the abstract by Rojas-Corrales et al. [Journal of Psychopharmacology 18(3):404-411 (2004)] wherein it is demonstrated that Tramadol "has an effect comparable to clinically effective antidepressants in a test predictive of antidepressant activity, without behavioural implications [and] has an inherent antidepressant-like (mood-improving) activity. Therefore the prior art of Bar-Or teaches that the prior art recognized many alternatives to treating premature ejaculation using antidepressants. Tramadol is one of those alternatives that may be selected based on what is effective in a given patient.

However, Crenshaw et al. teach an exact dosage of fluoxetine which is explicitly indicated for male human patient premature ejaculation (see abstract).

Accordingly, the specific dosages as disclosed for fluoxetine, a well-established antidepressant, are about 5 milligrams to about 80 milligrams for a time period of at least about 3

months, and preferably for time period of at least about 6 months.[…]. A daily dose of about 20 milligrams is preferred (column 3, lines 10-18). Exemplifications of the variability in dosing are further elucidated in the rest of column 3 of the instant specification.

Crenshaw et al. teach [that] [f]or the treatment contemplated by the present invention, […], other routes of administration [teach that], e.g., parenteral, by suppositories, buccal dosage forms, ***skin patch, and the like, can also be utilized.*** (col. 2 lines 64-68). Thus the skin patch constitutes a transdermal dressing which therefore also constitutes a local administration to at least a part of the male genitalia. The limitation drawn to *"and the like"* constitutes any extrapolation reasonably conceived by the one of skill in view of the scope and content of the invention.

Crenshaw does not expressly teach the limitations of claims 70-74. However, in this instance, applicants' attention are directed to obviousness in combining active agents which exemplify the same resulting effect on a disease, disorder, and/or condition such as premature ejaculation. In the instance of the alleged invention, it would be obvious to combine an SSRI with a newer antidepressant on the market such as MAOI to achieve greater therapeutic efficacy.

Claims 78, 80, 82, 83, and 84 is rejected under 35 U.S.C. 103(a) as being unpatentable over Bar-Or (USPGPUB 2002/0132857 A1) in view of Crenshaw et al. (USPN 5151448) and in further view of Rojas et al. as applied to claims 62-63 and 69-75 above, and further in view of Bodor et al (USPN 5024998).

Bar-Or in view of Crenshaw and/or Rojas et al. do not teach a medicament comprising of a serotonin reuptake inhibitor and MAO-inhibitors. They also do not teach the claimed enhancers

such as cyclodextrin.Bodor et al teach that the **cyclodextrin complexes** of the invention are preferably administered in the form of a pharmaceutical composition comprising the selected complex and a nontoxic pharmaceutically acceptable carrier therefor. Suitable nontoxic pharmaceutically acceptable carriers for use with the topic complexes, e.g., those less toxic than the target drug species themselves, will be apparent to those skilled in this art. [...] Obviously, the choice of suitable carriers will depend upon the route of administration and the exact nature of the particular dosage form selected, as well as upon the identity of the active drug species, the redox derivative and the complex to be administered. Contemplated routes of administration for the complexes of the invention include oral, buccal, sublingual, topical (including ophthalmic), rectal, ***vaginal, nasal***, and parenteral (including intravenous, intramuscular and subcutaneous).

In column 7 at lines 43-49, Bodor teaches aqueous media by which the active agents may be dissolved

Further, Bodor teaches antidepressants in column 18 line 58 and in column 23 at lines 49 and 59-60, respectively.

Bodor specifically teach that these embodiments of formulations drawn to the composition is designed for **nasal, vaginal,** or rectal administration, i.e. a nonoral or noninjectable route of administration is used Please see column 5 (underneath remainder of table beginning with Tuttle (incorporated by reference).

Further, in column 23 at lines 24 and 25, Bodor teaches MAO inhibitors.

Accordingly, Bodor teaches fluoxetine, a well-established and art-known serotonin reuptake inhibitor in column 24 at line 22.

MPEP cites:

2144.06 [R-6] Art Recognized Equivalence for the Same Purpose

I. COMBINING EQUIVALENTS KNOWN FOR THE SAME PURPOSE

"It is prima facie obvious to combine two compositions each of which is taught by the prior art to be useful for the same purpose, in order to form a third composition to be used for the very same purpose.... [T]he idea of combining them flows logically from their having been individually taught in the prior art." *In re Kerkhoven. , 626 F.2d 846, 850, 205 USPQ 1069, 1072 (CCPA 1980)*

As for the limitations drawn to via the combination of nasal and local administration, the contemplation to optimize therapy is reasonably identified via the disclosure of Bar-Or with Bodor providing additional motivation based upon the nature of the formulation comprising cyclodextrin (HPBCD), *supra.* Based upon the nature of the art, it would have been apparent and prima facie obvious to the one of skill to optimize the characterization of such therapy to achieve satisfaction and/or the desired effect.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event,

however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

***Conclusion***

Any inquiry concerning this communication or earlier communications from the examiner should be directed to TIMOTHY E. BETTON whose telephone number is (571)272-9922. The examiner can normally be reached on Monday-Friday 8:30a - 5:00p.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreeni Padmanabhan can be reached on (571) 272-0629. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

TEB

/SREENI PADMANABHAN/

Supervisory Patent Examiner, Art Unit 1617